

JournalScan

Iqbal Malik, Editor



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ISCHAEMIC HEART DISEASE

Another new risk marker in coronary heart disease

► After a spate of new inflammatory markers that appear to predict risk, this study of a very high risk population of patients (8% death rate at 12 months) having coronary angiography, suggests that having low levels of endothelial progenitor cells in your blood elevates cardiovascular risk. After adjustment for age, sex, vascular risk factors, and other relevant variables, increased levels of endothelial progenitor cells were associated with a reduced risk of death from cardiovascular causes (hazard ratio (HR) 0.31, 95% confidence interval (CI) 0.16 to 0.63; $p = 0.001$), a first major cardiovascular event (HR 0.74, 95% CI 0.62 to 0.89; $p = 0.002$), revascularisation (HR 0.77; 95% CI 0.62 to 0.95; $p = 0.02$), and hospitalisation (HR 0.76, 95% CI 0.63 to 0.94; $p = 0.01$). Endothelial progenitor cell levels were not predictive of MI or of death from all causes. This marker is not yet ready for "prime time".

▲ Werner N, Kosiol S, Schiegl T, *et al.* Circulating endothelial progenitor cells and cardiovascular outcomes. *N Engl J Med* 2005;353:999–1007.

An invasive strategy for ACS produces better long term health

► A total of 1810 patients (from 45 hospitals in England and Scotland, UK) with non-ST elevation acute coronary syndrome (ACS) were randomly assigned to receive an early intervention ($n = 895$) or a conservative strategy ($n = 915$) within 48 hours of the index episode of cardiac pain. In each group, the aim was to provide the best medical treatment, and also to undertake coronary arteriography within 72 hours in the interventional strategy with subsequent management guided by the angiographic findings. At one year follow up, rates of death or non-fatal myocardial infarction (MI) were similar. However, at a median of five years' follow up, 142 (16.6%) patients with intervention treatment and 178 (20.0%) with conservative treatment died or had non-fatal MI (odds ratio (OR) 0.78, 95% CI 0.61 to 0.99; $p = 0.044$), with a similar benefit for cardiovascular death or MI (0.74, 95% CI 0.56 to 0.97; $p = 0.030$). The benefits of an intervention strategy were mainly seen in patients at high risk of death or MI ($p = 0.004$), and for the highest risk group, the odds ratio of death or non-fatal MI was 0.44 (95% CI 0.25 to 0.76).

▲ Fox KAA, Poole-Wilson P, Clayton TC, *et al.* 5-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. *Lancet* 2005;366:914–20.

Choosing patients for invasive treatment after ACS

► Current guidelines recommend an early invasive strategy for patients who have acute coronary syndromes without ST segment elevation and with an elevated cardiac troponin T value. A total of 1200 patients with ACS without ST segment elevation who had chest pain, an elevated cardiac troponin T value ($\geq 0.03 \mu\text{g/l}$), and either electrocardiographic evidence of ischaemia at admission or a documented history of coronary disease were allocated to an early invasive strategy or to a more conservative (selectively invasive) strategy. Patients received modern treatment (aspirin, enoxaparin for 48 hours, and abciximab at the time of percutaneous coronary intervention). The use of clopidogrel and intensive lipid lowering therapy was recommended. The primary end point was a composite of death, non-fatal MI, or rehospitalisation for anginal symptoms within one year after randomisation. The estimated cumulative rate of the primary end point was 22.7% in the group assigned to early invasive management and 21.2% in the group assigned to selectively invasive management (relative risk (RR) 1.07, 95% CI 0.87 to 1.33; $p = 0.33$). The mortality rate was the same in the two groups (2.5%). MI was significantly more frequent in the group assigned to early invasive management (15.0% v 10.0%,

$p = 0.005$), but rehospitalisation was less frequent in that group (7.4% v 10.9%, $p = 0.04$). Why the lack of benefit? Over 50% of the conservative arm got revascularisation by one year, and the event rate overall was much lower than expected. MI was defined as any creatine kinase (CK) rise (after intervention or not) and most of the excess in the invasive arm was periprocedural rises, the significance of which is debated. It would be useful to update the meta-analysis of invasive versus selective invasive strategies including this study.

▲ de Winter RJ, Windhausen F, Cornel JH, *et al.* for the Invasive versus Conservative Treatment in Unstable Coronary Syndromes (ICTUS) Investigators. Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med* 2005;353:1095–104.

Use of a hands-free mobile phone is just as bad as a hands-on one

► Cardiologists love to talk. In the car is not the place, however. Driver's use of a mobile phone up to 10 minutes before a crash was associated with a fourfold increased likelihood of crashing (OR 4.1, 95% CI 2.2 to 7.7, $p < 0.001$). Risk was raised irrespective of whether or not a hands-free device was used (hands-free: OR 3.8, 95% CI 1.8 to 8.0, $p < 0.001$; hand held: OR 4.9, 95% CI 1.6 to 15.5, $p = 0.003$). Increased risk was similar in men and women and in drivers aged ≥ 30 and < 30 years. A third ($n = 21$) of calls before crashes and on trips during the previous week were reportedly on hand held phones.

▲ McEvoy SP, Stevenson MR, McCartt AT, *et al.* Role of mobile phones in motor vehicle crashes resulting in hospital attendance: a case-crossover study. *BMJ* 2005;331:428.

HYPERTENSION

Newer antihypertensive agents may be better than older ones

► The apparent shortfall in prevention of coronary heart disease (CHD) noted in early hypertension trials has been attributed to disadvantages of the diuretics and β blockers used. For a given reduction in blood pressure, some suggested that newer agents would confer advantages over diuretics and β blockers. ASCOT was a multicentre, prospective, randomised controlled trial in 19 257 patients with hypertension who were aged 40–79 years and had at least three other cardiovascular risk factors. Patients were assigned to either amlodipine 5–10 mg adding perindopril 4–8 mg as required (amlodipine based regimen; $n = 9639$), or atenolol 50–100 mg adding bendroflumethiazide 1.25–2.5 mg and potassium as required (atenolol based regimen; $n = 9618$). The primary end point was non-fatal MI (including silent MI) and fatal CHD. Analysis was by intention to treat. The study was stopped prematurely after 5.5 years' median follow up and accumulated in total 106 153 patient-years of observation. Though not significant, compared with the atenolol based regimen, fewer individuals on the amlodipine based regimen had a primary end point (429 v 474: unadjusted hazard ratio (HR) 0.90, 95% CI 0.79 to 1.02; $p = 0.1052$). There were reductions in fatal and non-fatal stroke (327 v 422: HR 0.77, 95% CI 0.66 to 0.89; $p = 0.0003$), total cardiovascular events and procedures (1362 v 1602: HR 0.84, 95% CI 0.78 to 0.90; $p < 0.0001$), and all cause mortality (738 v 820: HR 0.89, 95% CI 0.81 to 0.99; $p = 0.025$). The incidence of developing diabetes was less on the amlodipine based regimen (567 v 799: HR 0.70, 95% CI 0.63 to 0.78; $p = 0.0001$). This suggests that the amlodipine based regimen may have had some advantage beyond hypertension control, although adjustments for blood pressure control and other factors made the differences non-significant.

▲ Dahlöf B, Sever PS, Poulter NR, *et al.* Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian cardiac outcomes trial-blood pressure lowering arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet* 2005;366:895–906.

▲ Poulter NR, Wedel H, Dahlöf B, *et al.* Role of blood pressure and other variables in the differential cardiovascular event rates noted in the Anglo-Scandinavian cardiac outcomes trial-blood pressure lowering arm (ASCOT-BPLA). *Lancet* 2005;366:907–13.

GENERAL CARDIOLOGY

Vasodilator treatment does not reduce the need for AV replacement in patients with aortic regurgitation ► The authors randomly assigned 95 patients with asymptomatic severe aortic regurgitation and normal left ventricular function to receive open label nifedipine (20 mg every 12 hours), open label enalapril (20 mg per day), or no treatment (control group) to identify the possible beneficial effects of vasodilator treatment on left ventricular function and the need for aortic valve replacement. After a mean of seven years of follow up, the rate of aortic valve replacement was similar among the groups: 39% in the control group, 50% in the enalapril group, and 41% in the nifedipine group ($p = 0.62$). In addition, there were no significant differences among the groups in aortic regurgitant volume, left ventricular size, left ventricular mass, mean wall stress, or ejection fraction. One year after valve replacement, the left ventricular end diastolic diameter and end systolic diameter had decreased to a similar degree among the patients who underwent surgery in each of the three groups, and all the patients had a normal ejection fraction. So, long term vasodilator treatment with nifedipine or enalapril did not reduce or delay the need for aortic valve replacement in patients with asymptomatic severe aortic regurgitation and normal left ventricular systolic function.

▲ Evangelista A, Tornos P, Sambola A, *et al.* Long-term vasodilator therapy in patients with severe aortic regurgitation. *N Engl J Med* 2005;353:1342-9.

Cholesterol lowering is good for all ► In over 90 000 patients in 18 randomised trials of lipid lowering therapy, during a mean of five years, there were 8186 deaths, 14 348 individuals had major vascular events, and 5103 developed cancer. Mean low density lipoprotein (LDL) cholesterol differences at one year ranged from 0.35 mmol/l to 1.77 mmol/l (mean 1.09 mmol/l) in these trials. There was a 12% proportional reduction in all cause mortality per mmol/l reduction in LDL cholesterol (rate ratio 0.88, 95% CI 0.84 to 0.91; $p < 0.0001$). This reflected a 19% reduction in coronary mortality (0.81, 95% CI 0.76 to 0.85; $p < 0.0001$), and

non-significant reductions in non-coronary vascular mortality (0.93, 95% CI 0.83 to 1.03; $p = 0.2$) and non-vascular mortality (0.95, 95% CI 0.90 to 1.01; $p = 0.1$). There were corresponding reductions in MI or coronary death (0.77, 95% CI 0.74 to 0.80; $p < 0.0001$), in the need for coronary revascularisation (0.76, 95% CI 0.73 to 0.80; $p < 0.0001$), in fatal or non-fatal stroke (0.83, 95% CI 0.78 to 0.88; $p < 0.0001$), and, combining these, of 21% in any such major vascular event (0.79, 95% CI 0.77 to 0.81; $p < 0.0001$). The proportional reduction in major vascular events differed significantly ($p < 0.0001$) according to the absolute reduction in LDL cholesterol achieved, but not otherwise. These benefits were significant within the first year, but were greater in subsequent years. Taking all years together, the overall reduction of about one fifth per mmol/l LDL cholesterol reduction translated into 48 (95% CI 39 to 57) fewer participants having major vascular events per 1000 among those with pre-existing CHD at baseline, compared with 25 (95% CI 19 to 31) per 1000 among participants with no such history. There was no evidence that statins increased the incidence of cancer overall (1.00, 95% CI 0.95 to 1.06; $p = 0.9$) or at any particular site.

▲ Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005;366:1267-1278.

Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

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IMAGES IN CARDIOLOGY

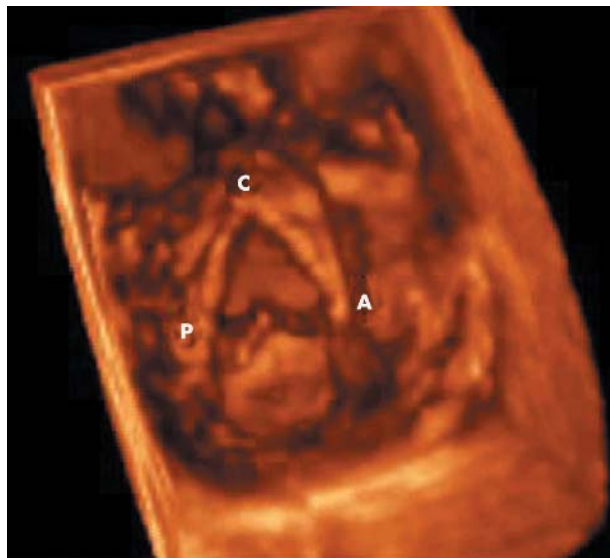
doi: 10.1136/hrt.2005.066456

Cleft mitral valve assessed by transthoracic real time three dimensional echocardiography

A 6 year old girl with apical systolic murmur underwent transthoracic two dimensional colour Doppler echocardiography. An isolated mild mitral regurgitation was noticed. The mitral regurgitant jet emanated through the anterior mitral valve. The left ventricle was not dilated with normal shortening fraction. Real time three dimensional echocardiography (Sonos 7500, Philips) was performed using the matrix probe (2-4 MHz). A full volume was acquired from an apical window with ECG monitoring. En face view of the mitral valve was obtained immediately. The asymptomatic patient was followed up without surgical indication.

S Abadir
Y Dulac
A Taktak
P Acar

acar.p@chu-toulouse.fr



Three dimensional en face view of the mitral valve. The valve is viewed from below. The anterior mitral valve is divided into two equivalent leaflets by a cleft (C). The anterior (A) and posterior (P) commissures as well as the papillary muscles underneath are clearly seen delimitating the posterior mitral valve.